

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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Applicant's or agent's file reference 99473 WO	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP00/03747	International filing date (day/month/year) 25/04/2000	Priority date (day/month/year) 29/04/1999
International Patent Classification (IPC) or national classification and IPC A61K31/58		
Applicant AKZO NOBEL N.V.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 28/11/2000	Date of completion of this report 31.08.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Giacobbe, S Telephone No. +49 89 2399 8463 

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/03747

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17):*):

**Description, pages:**

1-9 as originally filed

**Claims, No.:**

1-9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/03747

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

## III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 8, 9 (IA only).

because:

- ☒ the said international application, or the said claims Nos. 8, 9 (IA only) relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
  - ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
  - ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
  - ☐ no international search report has been established for the said claims Nos. .
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the standard.
  - ☐ the computer readable form has not been furnished or does not comply with the standard.

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1,2,4,5,7-9
	No: Claims 3,6
Inventive step (IS)	Yes: Claims 1,2,4,5,7-9
	No: Claims 3,6
Industrial applicability (IA)	Yes: Claims 1-7,9

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP00/03747

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No: Claims 8 (see Separate Sheet)

2. Citations and explanations  
see separate sheet

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
see separate sheet

## **1. Section III**

Claim 8 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT). However, although not required under the provisions of the PCT, an opinion will be given with respect to novelty and inventive step.

## **2. Section V**

### **2.1 Cited Documents**

2.1a The following documents (D) are referred to in this Report:

- D1: WO 94 04156 A (AKZO N.V.) 3 March 1994
- D2: WO 93 21927 A (MEDICAL COLLEGE OF HAMPTON ROADS) 11 November 1993
- D3: WO 97 49407 A (AKZO NOBEL N.V.) 31 December 1997
- D4: SCHOONEN W.G.E. ET AL: 'Human progesterone receptor A and B isoforms in CHO cells. II. Comparison of binding, transactivation and EDD50 values of several synthetic (anti)progestagens in vitro in CHO and MCF-7 cells and in vivo in rabbits and rats' J. STEROID BIOCHEM. MOL. BIOL., vol. 64(3), 1998, pages 157-170

Unless otherwise indicated reference is made to the passages cited in the Search Report.

2.1b The content of the cited documents is the following:

- i) document D1 discloses the combination of a multi-phase progestin preparation and preferentially 14 sequential dosage units of a anti-progestin compound, e.g. Org 33245, for use in contraception. Decreased bleeding is mentioned as additional advantage (cf. p. 2, l. 33);
- ii) document D2 discloses regimens of progestin-only preparations and intermittent anti-progestin, e.g. once every 30 days. Org 31710 is explicitly mentioned as a preferred anti-progestin. Decreased bleeding is mentioned as additional advantage (cf. p. 3, ll. 13-17);
- iii) document D3 discloses regimens of progestin-only preparations and

intermittent anti-progestin, e.g. twice every 30 days for use as contraceptive and/or for HRT. Org 31710 is explicitly mentioned as a preferred anti-progestin. Decreased bleeding is mentioned as additional advantage (cf. p. 2, ll. 13-16);

iv) in document D4 the anti-progestinic activity of Org 33245 is compared to that of Org 31710, in vitro and in vivo. It is shown that the former is more active than the latter.

## **2.2 Art 33(2) PCT (Novelty)**

The subject-matter of present claims 3 and 6 does not meet the requirements of Art 33(2) PCT since it is anticipated by the disclosure of document D1.

**n.b.** Contraception is not considered as a method of treatment of the body by therapy, since pregnancy is not a disease. Therefore a claim formulated following the Swiss format (i.e. claims 1-4) are considered as directed to a non-medical use of the named compositions and therefore as not-novel if the compositions themselves are known. Claim 7 (and 9, as far as it refers to 7) are considered as non-medical method claims.

## **2.3 Art 33(3) PCT (Inventive step)**

The subject-matter of present claims 1, 2, 4, 5 and 7-9 does not meet the requirements of Art 33(3) PCT.

Documents D2 and D3 constitute the closest prior art. The technical problem to be solved can be formulated as "how to find a contraceptive preparation alternative to that of D2 and D3". The disclosure of document D4 clearly suggests to the skilled person as a possible solution the use Org 33245 instead of Org 31710, thereby rendering the subject-matter of the aforementioned claims obvious.

## **2.4 Art 33(4) PCT (Industrial applicability)**

As stated above, no opinion is given on the question of whether present claim 8 is industrially applicable since its patentability is inter alia dependent upon its formulation as well as upon national and regional laws and no unifying criteria is provided in this field by the PCT.

## **3. Section VIII**

The term "intermittent" in claims 5 and 7-9 is not clear.

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

Date of mailing (day/month/year) 09 January 2001 (09.01.01)	
International application No. PCT/EP00/03747	Applicant's or agent's file reference 99473 WO
International filing date (day/month/year) 25 April 2000 (25.04.00)	Priority date (day/month/year) 29 April 1999 (29.04.99)
Applicant COELINGH BENNINK, Herman, Jan, Tijmen et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
 28 November 2000 (28.11.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer R. E. Stoffel
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

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(19) World Intellectual Property Organization  
International Bureau



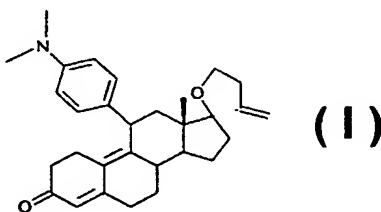
(43) International Publication Date  
9 November 2000 (09.11.2000)

PCT

(10) International Publication Number  
**WO 00/66129 A3**

- (51) International Patent Classification<sup>7</sup>: **A61K 31/58** (NL). SCHOONEN, Wilhelmus, Gerardus, Eduardus, Joseph [NL/NL]; Parklaan 16, NL-5345 BV Oss (NL).
- (21) International Application Number: **PCT/EP00/03747**
- (22) International Filing Date: **25 April 2000 (25.04.2000)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:  
99201390.4 29 April 1999 (29.04.1999) EP
- (71) Applicant (for all designated States except US): **AKZO NOBEL N.V.** [NL/NL]; Velperweg 76, NL-6824 AB Arnhem (NL).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **COELINGH BEN-NINK, Herman, Jan, Tijmen** [NL/NL]; Melvill van Carnbeelaan 38, NL-3971 BE Driebergen (NL). **DECKERS, Godefridus, Hermanus, Johanna** [NL/NL]; van Limburg Stirumstraat 34, NL-5344 HW Oss (NL). **DOLS, Paul, Peter, Marie, Antonius** [NL/NL]; Ringelenburg 1, NL-5346 VR Oss (NL). **ORLEMANS, Everardus, Otto, Maria** [NL/NL]; Wolfespoor 12, NL-5343 XM Oss
- (74) Agent: **KRAAK, Hajo**; P.O. Box 20, NL-5340 BH Oss (NL).
- (81) Designated States (national): **AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA.**
- (84) Designated States (regional): **ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).**
- Published:  
— With international search report.
- (88) Date of publication of the international search report:  
19 April 2001
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **USE OF ANTIPROGESTAGENS IN COMBINED THERAPY**



(57) Abstract: It has been found that the compound satisfying the structural formula (I) given below has a surprisingly good suitability for being administered intermittently. This particular compound therewith has the highly advantageous property that it can be used in the specific medical application of combined therapy with progestagen-only preparations.

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Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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EE	Estonia						

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## INTERNATIONAL SEARCH REPORT

Application No

/EP 00/03747

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61K31/58

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 94 04156 A (AKZO N.V.) 3 March 1994 (1994-03-03)	6,7
A	page 3, line 20-22; claims 1,4,8 page 2, line 9,10 page 3, line 36-38	1,2,4,5
Y	WO 93 21927 A (MEDICAL COLLEGE OF HAMPTON ROADS) 11 November 1993 (1993-11-11) cited in the application page 4, line 26-34; claims 1-5,9-16,20,21 page 9, line 32-35 page 10, line 12-17 page 7, line 20-31	1-9
	-/--	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

20 December 2000

Date of mailing of the international search report

29/12/2000

Name and mailing address of the ISA

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Authorized officer

Kanbier, D

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## INTERNATIONAL SEARCH REPORT

of Application No

EP 00/03747

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 97 49407 A (AKZO NOBEL N.V.) 31 December 1997 (1997-12-31) cited in the application page 2, line 18-28; claims 1-4,9,10 page 4, line 5-9	1,2,4-7, 9
Y	SCHOONEN W.G.E. ET AL: "Human progesterone receptor A and B isoforms in CHO cells. II. Comparison of binding, transactivation and EDD50 values of several synthetic (anti)progestagens in vitro in CHO and MCF-7 cells and in vivo in rabbits and rats" JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, vol. 64, no. 3, 1998, pages 157-170, XP002124156 United Kingdom page 164, right-hand column -page 165 page 167, right-hand column, line 1-4	1,3,5-8
A	WO 93 17686 A (SCHERING AG) 16 September 1993 (1993-09-16) page 4, line 14-16 page 5, line 28-36 page 7, line 3-7 page 10, line 19-23 page 9, line 31 -page 10, line 9	1,2,4-9
A	EP 0 549 041 A (AKZO N.V.) 30 June 1993 (1993-06-30) cited in the application claim 6; example 1	1,3,5-8

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No  
EP 00/03747

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9404156 A	03-03-1994	AU 4708993 A MX 9304931 A ZA 9305617 A	15-03-1994 31-08-1994 07-03-1994
WO 9321927 A	11-11-1993	WO 9321926 A AT 187644 T AU 1918092 A AU 4368593 A CA 2131911 A CN 1079651 A DE 69327319 D DE 69327319 T DK 646008 T EP 0646008 A ES 2142345 T FI 945207 A GR 3032797 T JP 8509456 T NO 944210 A NZ 253405 A PT 646008 T US 5622943 A ZA 9303153 A	11-11-1993 15-01-2000 29-11-1993 29-11-1993 11-11-1993 22-12-1993 20-01-2000 13-07-2000 15-05-2000 05-04-1995 16-04-2000 04-11-1994 30-06-2000 08-10-1996 04-11-1994 24-06-1997 28-04-2000 22-04-1997 06-12-1993
WO 9749407 A	31-12-1997	AU 725670 B AU 3436097 A BR 9709934 A CZ 9804289 A EP 0912186 A NO 986104 A NZ 332894 A PL 330916 A	19-10-2000 14-01-1998 10-08-1999 11-08-1999 06-05-1999 23-12-1998 28-05-1999 07-06-1999
WO 9317686 A	16-09-1993	CN 1079386 A AU 678150 B BR 9306005 A CA 2134961 A CZ 9402111 A EP 0630246 A FI 944022 A IL 104915 A JP 7509218 T MX 9301121 A NO 943234 A NZ 268304 A PL 174785 B PL 172790 B SK 104694 A ZA 9301492 A AU 3787993 A RU 2127112 C	15-12-1993 22-05-1997 23-06-1998 03-09-1993 13-12-1995 28-12-1994 01-09-1994 15-07-1998 12-10-1995 01-09-1993 01-11-1994 24-02-1997 30-09-1998 28-11-1997 10-01-1996 23-12-1993 05-10-1993 10-03-1999
EP 549041 A	30-06-1993	AT 128983 T AU 655858 B AU 3009392 A CA 2084431 A DE 69205405 D DE 69205405 T	15-10-1995 12-01-1995 24-06-1993 21-06-1993 16-11-1995 09-05-1996

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## INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte

Application No

EP 00/03747

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 549041	A	DK 549041 T	29-01-1996
		ES 2081040 T	16-02-1996
		FI 925790 A	21-06-1993
		GR 3018630 T	30-04-1996
		HK 1002033 A	24-07-1998
		JP 5255380 A	05-10-1993
		MX 9207394 A	30-07-1993
		NO 302525 B	16-03-1998
		NZ 245520 A	24-02-1995
		US 5292878 A	08-03-1994
		ZA 9209315 A	24-05-1993

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